UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

IN RE: ZOFRAN (ONDANSETRON) PRODUCTS LIABILITY LITIGATION	)	**MDL No. 1:15-md-2657-FDS**
This Document Relates To:	)	
ALEKSANYAN v. GLAXOSMITHKLINE LLC, 1:19-cv-10603, et al.[1]	)	

MEMORANDUM AND ORDER ON DEFENDANT'S MOTION FOR SUMMARY JUDGMENT BASED ON LACK OF GENERAL CAUSATION EVIDUENCE

SAYLOR, J.

This is a multi-district litigation ("MDL") proceeding arising out of product-liability claims that the use of the drug Zofran (ondansetron) by pregnant women caused certain types of birth defects in their children.

Defendant GlaxoSmithKline LLC ("GSK") has moved for summary judgment in 72 individual cases based on lack of general-causation evidence that Zofran can cause injuries other

[1] This document relates to the following cases: Aleksanyan (19-cv-10603); Arellanes (15-cv-13743); Betschart (16-cv-11042); Birt (15-cv-13740); Bivens (17-cv-10286); Black (17-cv-10953); Blair (16-cv-11140); Blas (15-cv-14065); Boswell (15-cv-13940); Boyack (18-cv-11874); Cameron (16-cv-12111); Crowell (17-cv-12389); Cruz (17-cv-10167); Cummings (15-cv-13775); Curington (15-cv-13889); Daniels (18-cv-11081); Davis (16-cv-10825); De la Cruz (17-cv-10372); Echols (15-cv-13759); Fair (17-cv-10755); Fuentez (17-cv-10676); Goodwin (15-cv-13828); Green (16-cv-10720); Griffin (17-cv-11890); Griffin-Sperbeck (17-cv-10097); Guzman (17-cv-11035); Hall (17-cv-12394); Hernandez (17-cv-10277); Hill (16-cv-12388); Ingham (19-cv-10698); Johnson (17-cv-11274); Jones (16-cv-11518); Kennelly (18-cv-10825); Killpack (17-cv-10336); Koontz (17-cv-10957); Lambeth (15-cv-13931); Lara (16-cv-10198); Larson (16-cv-11829); Leath (15-cv-13917); Lee (17-cv-10592); Lowery (17-cv-11854); Mandoyan (15-cv-13564); Marlenee (15-cv-13585); Mauss (16-cv-10469); Mayo (15-cv-13207); McGee (18-cv-12272); Meads (17-cv-12579); Michael (17-cv-12389); Mirandola (16-cv-11440); Myint (18-cv-10149); Newman (15-cv-13974); Nicholson (17-cv-11490); Ortiz (18-cv-10703); Parden (15-cv-13973); Poe (15-cv-13937); Powell (18-cv-10775); Printz (17-cv-10099); Ray (15-cv-14103); Roberts (15-cv-13710); Scangarello (18-cv-11085); Schacht (15-cv-14085); Schmitt (17-cv-11960); Shepherd (18-cv-10973); Smith (17-cv-10981); Southerland (16-cv-10197); Stacy (17-cv-10350); Swaim (15-cv-14122); Titus (15-cv-14148); Wentz (16-cv-12467); Wilkinson (15-cv-13920); Wilkinson (19-cv-10270); Zgurski (15-cv-14038).

than cardiac defects and isolated cleft palate.

For the following reasons, the motion will be granted as to plaintiffs Boswell (15-cv-13940), Griffin-Sperbeck (17-cv-10097), Guzman (17-cv-11035), Jones (16-cv-11518), and Mandoyan (15-cv-13564), and will otherwise be denied.

I. Background

A. Factual Background

GlaxoSmithKline LLC ("GSK") is a pharmaceutical company. (Master Long Form Complaint-Brand Zofran Use (Docket No. 255) ("Compl.") ¶¶ 2-3). Until March 23, 2015, GSK manufactured and sold Zofran, or ondansetron. (*Id.* ¶ 6).

Zofran is an anti-emetic—that is, a drug that prevents or treats nausea or vomiting. (*Id.* ¶ 17). In 1991, it was approved for marketing in the United States for the prevention of nausea and vomiting induced by chemotherapy or radiation therapy and post-operative nausea and vomiting. (*Id.* ¶¶ 16, 23).

The plaintiffs in this MDL proceeding are parents and guardians of children who allege that they were born with birth defects caused by prenatal exposure to Zofran. (*Id.* ¶ 1). According to plaintiffs, pre-clinical studies conducted by or on behalf of GSK in the 1980s revealed that Zofran ingested by mammals—in particular, rats and rabbits—during pregnancy crosses the placental barrier, exposing the fetus to the drug. (*Id.* ¶ 43). Plaintiffs contend that subsequent scientific research has confirmed that Zofran also crosses the placental barrier during human pregnancies. (*Id.* ¶ 44). As a result, plaintiffs allege, Zofran's established side effects can occur in human embryos and fetuses, leading to birth defects. (*Id.* ¶ 40).

The parties have conducted extensive expert discovery on the issue of general causation—that is, whether and how Zofran can cause the type of injuries suffered by plaintiffs.

Plaintiffs have submitted general causation reports from five experts: Dr. Bengt R.

Danielsson, a physician and teratologist; Dr. Carol Louik, an epidemiologist; Dr. Michael Levin, a biologist; Dr. Ra-id Abdulla, a pediatric cardiologist; and Dr. Thomas W. Sadler, an embryologist, developmental biologist, and teratologist. Several of these experts have opined that, based on their respective expertise and review of the data relevant in their field, Zofran can cause cardiac and orofacial birth defects. (Danielsson Report at 68; Levin Report at 6; Sadler Report at 6). Orofacial defects are those that occur in and around the facial region, including specific defects such as cleft palate. (*See* Sadler Report at 23).

GSK has submitted general causation reports by its own experts, who have opined that the available medical evidence does not support a causal connection between Zofran and any type of birth defects. (*See, e.g.*, Shaw Report at 1; Kimmel Report at 3; Baldwin Report at 3).[2]

B. The Present Motion

On June 11, 2019, GSK moved for summary judgment based on lack of general-causation evidence in 72 individual cases. The plaintiffs in those cases allege that Zofran caused injuries other than heart defects and isolated cleft palate—that is, cleft palate in the absence of any other orofacial injuries. GSK contends that those 72 plaintiffs have provided no scientific evidence that Zofran can cause the types of injuries they suffered.

Since GSK filed the motion, 14 of those cases have been voluntarily dismissed. (GSK's Reply (Docket No. 1672), Ex. 1). Plaintiffs have filed an omnibus opposition in 48 cases that allege orofacial injuries. (*Id.*). Two plaintiffs have opposed the motion individually: Powell (18-cv-10775) and Scangarello (18-cv-11085). (*Id.*). GSK has withdrawn its motion as to one plaintiff: Michaels (17-cv-12389). (17-cv-12389, Docket No. 42). Five plaintiffs have not

[2] Both plaintiffs and GSK have moved to exclude the testimony of each other's experts under Fed. R. Evid. 702 and *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 593-95 (1993). (*See* Pls.' Mot. to Exclude Causation Opinions (Docket No. 1251); GSK's Mot. to Exclude Pls.' Gen. Causation Experts (Docket No. 1310)). The Court held several days of hearings on those motions and has taken them under advisement.

opposed the motion: Boswell (15-cv-13940), Griffin-Sperbeck (17-cv-10097), Guzman (17-11035), Jones (16-cv-11518), and Mandoyan (15-cv-13564). (*Id.*).[3]

II. Legal Standard

The role of summary judgment is "to pierce the pleadings and to assess the proof in order to see whether there is a genuine need for trial." *Mesnick v. General Elec. Co.*, 950 F.2d 816, 822 (1st Cir. 1991) (quoting *Garside v. Osco Drug, Inc.*, 895 F.2d 46, 50 (1st Cir. 1990)). Summary judgment shall be granted when "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). A genuine issue is "one that must be decided at trial because the evidence, viewed in the light most flattering to the nonmovant . . . would permit a rational fact finder to resolve the issue in favor of either party." *Medina-Munoz v. R.J. Reynolds Tobacco Co.*, 896 F.2d 5, 8 (1st Cir. 1990) (citation omitted). In evaluating a summary judgment motion, the court indulges all reasonable inferences in favor of the nonmoving party. *See O'Connor v. Steeves*, 994 F.2d 905, 907 (1st Cir. 1993). When "a properly supported motion for summary judgment is made, the adverse party must set forth specific facts showing that there is a genuine issue for trial." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 250 (1986) (quotations omitted). The nonmoving party may not simply "rest upon mere allegation or denials of his pleading," but instead must "present affirmative evidence." *Id.* at 256-57.

III. Analysis

A. Causation Generally

"In order to prevail in a pharmaceutical personal injury case, a plaintiff must establish

[3] At plaintiff Boswell's request, the Court extended her deadline for filing a response to GSK's motion until August 2, 2019. (15-cv-13940, Docket No. 75). However, plaintiff has yet to file any response.

two types of causation: general and specific." *In re Neurontin Mktg., Sales Practices, & Prod. Liab. Litig.*, 612 F. Supp. 2d 116, 123 (D. Mass. 2009) (citing *In re Bextra and Celebrex Mktg. Sales Practices and Prod. Liab. Litig.*, 524 F. Supp. 2d 1166, 1171-72 (N.D. Cal. 2007); *In re Rezulin Prods. Liab. Litig.*, 369 F. Supp. 2d 398, 401-02 (S.D.N.Y. 2005)). "General causation is established by demonstrating, often through a review of scientific and medical literature, that exposure to a substance can cause a particular disease . . . . Specific, or individual, causation, however, is established by demonstrating that a given exposure is the cause of an individual's disease. . . ." *Id.* (quoting Mary Sue Henifin, et al., *Reference Guide on Medical Testimony*, *in* REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 439, 444 (Fed. Judicial Ctr. 2d ed. 2000); *see also* John B. Wong, et al., *Reference Guide on Medical Testimony*, in REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 687, 691 (Fed. Judicial Ctr. 3d ed. 2011). Only general causation—whether Zofran can cause injuries other than heart defects and isolated cleft palate—is at issue in this motion.

It is well-established under Massachusetts law that "expert testimony is required to establish medical causation." *Milward v. Rust-Oleum Corp.*, 820 F.3d 469, 476 (1st Cir. 2016) (quoting *Reckis v. Johnson & Johnson*, 471 Mass. 272, 292 (2015). "This applies to both general and specific causation." *Id.* (citing *Reckis* at 471 Mass. at 292 n.33).

B. Plaintiffs Boswell (15-cv-13940), Griffin-Sperbeck (17-cv-10097), Guzman (17-cv-11035), Jones (16-cv-11518), and Mandoyan (15-cv-13564)

Plaintiffs Boswell (15-cv-13940), Griffin-Sperbeck (17-cv-10097), Guzman (17-cv-11035), Jones (16-cv-11518), and Mandoyan (15-cv-13564) have not opposed the motion for summary judgment.

GSK submitted a statement of material facts along with this motion for summary judgment that shows that there is no study reporting a causal link between the ingestion of

Zofran and the development of cleft lip (with or without cleft palate) in the fetus. (GSK's SUF ¶¶ 2-4). It also shows that plaintiffs Boswell, Griffin-Sperbeck, Guzman, Jones, and Mandoyan all allege that Zofran caused injuries other than cardiac defects and isolated cleft palate. (*Id.* ¶¶ 13, 29-30, 36, 46).

Under Local Rule 56.1, plaintiffs were required to submit "a concise statement of the material facts of record as to which it is contended that there exists a genuine issue to be tried." Under that rule, any facts in GSK's statement of material facts that plaintiffs do not oppose by such a statement "will be deemed . . . admitted." Those five plaintiffs failed to submit such a statement, or to otherwise oppose the motion for summary judgment. The Court deems the facts set forth in GSK's statement of material facts admitted as to those five plaintiffs. As to those five plaintiffs, therefore there is no genuine issue of fact as to general causation—that is, whether Zofran could have caused these plaintiffs' injuries.

Accordingly, plaintiffs Boswell (15-cv-13940), Griffin-Sperbeck (17-cv-10097), Guzman (17-cv-11035), Jones (16-cv-11518), and Mandoyan (15-cv-13564) cannot establish that exposure to Zofran caused their alleged injuries. GSK's motion for summary judgment based on lack of general causation evidence will therefore be granted as to those plaintiffs.

C. Plaintiff Powell (18-cv-10775)

Plaintiff Samantha Powell alleges that her ingestion of Zofran while pregnant caused fatal heart defects in her child. (GSK's SUF ¶ 60; 18-cv-10775, Short Form Compl. at ¶ 10). Medical records show that Powell's child was diagnosed in utero with, among other things, trisomy 18 (a chromosomal abnormality that can independently cause heart defects) and "significant congenital heart disease," including double outlet right ventricle and ventricular septal defect. (POWELL -

318262 -9; *see also* 18-cv-10775, Short Form Compl. at ¶ 10).[4] Powell has opposed GSK's motion for summary judgment, contending that Zofran caused her child's structural heart defects, but not the trisomy 18.

GSK contends there is no evidence that Zofran can cause heart defects in a patient with the "constellation of defects" that Powell's child suffered. (July 10, 2019 Hr'g Tr. at 61:4-19). Specifically, it contends there is no evidence that Zofran can cause heart defects in a patient who also has omphalocele (a defect in the abdominal wall) or trisomy 18. (GSK's Reply at 8).

However, that argument conflates specific causation with general causation. Whether or not Zofran in fact caused heart defects in this particular child, in light of the child's other birth defects, is a question of specific causation. At this juncture, the only issue is whether Zofran can cause heart defects of the type that the child suffered, with or without the presence of any other defects.

Plaintiffs' experts have opined that Zofran can indeed cause congenital heart defects, including septal defects of the kind alleged. (*See* Danielsson Report at 67-68; Sadler Report at 31 (Zofran can cause septal defects); Louik Report at 40-41 (Zofran "can cause cardiac defects, specifically septal defects")). Because there is a genuine dispute of material fact as to whether Zofran can cause septal defects, and because Powell alleges that injury here, summary judgment on the issue of general causation is inappropriate.

Accordingly, GSK's motion for summary judgment will be denied as to Powell.

D. <u>Plaintiff Scangarello (18-cv-11085)</u>

Plaintiff Kristen Scangarello alleges that her ingestion of Zofran while pregnant caused

[4] There is an apparent inconsistency between Powell's short-form complaint and the medical records as to the type of defect suffered by her child. Powell's complaint says "ASD" (atrial septal defect), while the child's medical records say "VSD" (ventricular septal defect). The difference does not appear to be material for present purposes.

her child to suffer the following injuries: cleft palate, epilepsy, horseshoe kidney, ureter reflux, bilateral estropia, motor delay, and muscle hypotension. (GSK's SUF ¶ 64, GSK's Mem. in Supp., Ex. 65 (18-cv-11085, Plaintiff Fact Sheet) at Section F.8.a).

Scangarello has opposed GSK's motion for summary judgment, contending that her child was born with an isolated cleft palate. (Scangarello Opp. at 3). She submitted a declaration in which she states that "[o]ther than isolated cleft palate, [her child] has no other known orofacial defects." (*Id.*, Ex. 3 (Scangarello Decl.) ¶ 8).

GSK contends that there is no evidence that Zofran can cause the type of injuries alleged. It points out that the medical records indicate that her child suffered other defects of the head or face, including a "small chin from dysmorphic features" and a "small mandible," as well as a set of abnormalities known as Pierre Robin sequence, which is independently associated with cleft palate. (*See* GSK's Reply at 9-10; Scangarello Opp., Ex. 1 (8/11/2010 Medical Records)). It also contends that Scangarello may not avoid summary judgment by relying on her own self-serving declaration when it is contradicted by the medical records: although she claims that her child suffered no other orofacial defects other than a cleft palate, but her exhibits clearly show other defects of the head or face. (*See* GSK's Reply at 9-10).

Again, GSK is conflating issues of specific causation and general causation. Whether Zofran in fact caused the cleft palate in this child, in light of the child's other defects, is an issue of specific causation. The question at this stage is whether as a general matter Zofran can cause cleft palate injuries. It is true that Scangarello's declaration appears to contradict her child's medical records. But GSK has not cited any evidence that the orofacial defects are causally distinct from isolated cleft palate—that is, that the evidence indicating that Zofran can generally cause cleft palate does not apply to children who have Pierre-Robin Sequence, a small mandible,

or any of the other relevant orofacial defects. Thus, at this stage there is no reason, at least on the present record, to treat Scangarello's claim any differently from those of other plaintiffs alleging cleft palate.

Because there is a genuine dispute of material fact as to whether Zofran can cause cleft palate, and Scangarello alleges the existence of that injury here, summary judgment on the issue of general causation is inappropriate. Accordingly, GSK's motion for summary judgment will be denied as to Scangarello.

E. Other Plaintiffs

Finally, plaintiffs have filed an omnibus opposition in 48 cases alleging orofacial defects—specifically, defects of the palate *or* lip. (Pls.' Omnibus Mem. in Opp. at 3-4). GSK contends that there is no scientific evidence that Zofran can cause orofacial injuries other than isolated cleft palate. Specifically, it points to two sets of statements—a purported admission by plaintiffs' counsel and several statements by its experts—that it contends show a lack of general causation evidence for orofacial injuries other than isolated cleft palate.

1. Whether Plaintiffs' Counsel Made a Judicial Admission

First, GSK contends that plaintiffs have made a judicial admission that there is no evidence that Zofran can cause orofacial defects other than isolated cleft palate. Specifically, it cites to an excerpt from the *Daubert* Hearing on April 26, 2019:

> THE COURT: What about the defects that are not either cardiac or orofacial? What about – what's in that category? . . .
>
> [Plaintiffs' Counsel]: If there are defects outside of heart and palate, those – I don't know how the numbers tally up, but I will tell you that I don't believe the scientific evidence has caught up to proving these, if they are simply existing on an independent basis outside of a heart or a palate. . . .

(Apr. 26, 2019 Hr'g Tr. at 4-22:11-19). GSK argues that because plaintiffs' counsel admitted in a court proceeding that there is no evidence that Zofran can cause orofacial defects other than

cleft palate, plaintiffs should be held to that admission. *See United States v. Belculfine*, 527 F.2d 941, 944 (1st Cir. 1975) (explaining that "judicial admissions are conclusive on the party making them").

Taken in context, however, the statement by plaintiffs' counsel is not a clear concession as to defects not involving the palate. It is true that plaintiffs' counsel said there was insufficient evidence to prove Zofran causes defects "outside of a heart or a *palate*." (Apr. 26, 2019 Hr'g Tr. at 4-22:11-19) (emphasis added). But the Court had just asked about defects "that are not either cardiac or orofacial"—not about the difference between cleft palate and other orofacial injuries. (*Id.*). Given that context, it is unclear whether plaintiffs' counsel intended to say that scientific evidence of causation exists for only heart and orofacial injuries, rather than only heart and palate injuries.[5] And shortly before the disputed statement, plaintiffs' counsel had specifically asserted that there *was* evidence Zofran could indeed cause defects of the palate *or* lip. (*See id.* at 4-21:16-21).

"To be binding, a judicial admission must be clear." *Harrington v. City of Nashua*, 610 F.3d 24, 31 (1st Cir. 2010) (internal quotations omitted). It is far from a clear admission for counsel to assert clearly that there is evidence Zofran can cause orofacial injuries besides isolated cleft palate, and then to supposedly concede in the next minute—in an answer to a different question—that there is no such evidence. Accordingly, plaintiffs will not be deemed to have made a judicial admission that Zofran cannot cause facial injuries other than to the palate.

[5] GSK contends that plaintiffs' counsel should be expected to know the difference between palate-only injures and orofacial injuries more broadly because of his experience with this litigation, and to choose his words accordingly. While that may be true, the Court declines to attach such significant consequences to a single word used by counsel, on which the Court did not rely. *See Belculfine*, 527 F.2d at 944 ("Similarly, considerations of fairness and the policy of encouraging judicial admissions require that trial judges be given broad discretion to relieve parties from the consequences of judicial admission in appropriate cases.").

2. Whether Plaintiffs' Experts Conceded There Is Insufficient Evidence That Zofran Can Cause Orofacial Injuries Other than Cleft Palate

Next, GSK contends that two of plaintiffs' experts conceded at their depositions that there is no evidence Zofran can cause orofacial injuries other than isolated cleft palate. Those two experts are Dr. Thomas W. Sadler and Dr. Carol Louik.

a. Dr. Thomas W. Sadler

Dr. Thomas W. Sadler is an embryologist, developmental biologist, and teratologist. (Sadler Report at 1). He was retained by plaintiffs to opine as to whether Zofran can cause congenital birth defects, including heart and orofacial abnormalities. (*Id.*).

GSK contends Dr. Sadler admitted that there are "two orofacial phenotypes (1) cleft palate; and (2) cleft lip with or without cleft palate," which must be "examined separately" for causation purposes. (GSK's Mem. in Supp., 8 n.1). Specifically, GSK cites to the following exchange at his deposition on May 30, 2019:

> Q. . . . I think at your last deposition we established that there are, you know, two phenotypes of clefts, two major phenotypes of clefts. Right? There's cleft palate and then there's cleft lip with or without cleft palate. Correct?
>
> A. That's usually how they're classified, yes.
>
> Q. And I think we've established that they are pathogenetically and etiologically distinct. Right?
>
> A. Yes.

(May 30, 2019 Sadler Dep. at 169:8-19). GSK contends that because Dr. Sadler conceded that the two orofacial phenotypes were "pathogenetically and etiologically distinct," he admitted that there is only evidence that Zofran causes isolated cleft palate, and no evidence that it causes cleft lip with or without cleft palate. But that issue must be considered in the context of his earlier deposition.

That deposition took place on September 25, 2018. At first, Dr. Sadler denied that the

two phenotypes of orofacial defects were "etiologically distinct":

> Q. . . . I'm asking that – Is it fair to say that these two phenotypes – meaning cleft lip with or without cleft palate and cleft palate only – are etiologically distinct? And, by 'etiologically', I mean in terms of causation?
>
> A. I don't agree.

(Sep. 25, 2018 Sadler Dep. at 56:23-57:3). After that exchange, GSK's counsel produced a copy of Dr. Sadler's book on embryology and congenital malformations, part of which read: "These conditions are usually classified as with or without cleft palate and cleft palate, and are thought to be etiologically and pathogenetically distinct." (*Id.* at 57:4-58:10). He responded:

> A. That's not a definitive statement. And, if you read the next paragraph or the paragraph below the next paragraph, it says, "Causes of cleft lip with or without cleft palate are not well defined."
>
> Q. So let me –
>
> A. So that implies – or, at least from what I know about mechanisms of teratology – that you can get a cleft lip with or without a cleft palate and have the same mechanism – say . . .

(*Id.* at 58:12-20). Dr. Sadler went on to list several examples of such mechanisms. Then, counsel asked Dr. Sadler the following questions:

> Q. I think I understand exactly what you're saying. I think what you're saying is 00 [sic] and correct me, if I'm wrong – is that you can have the same exposure that can cause both cleft palate only and cleft lip with or without cleft palate – That's what you're saying, correct?
>
> A. Right. Based on—But you have to know what the mechanism is – which would mean the etiology, in my opinion.
>
> Q. But it's also correct to say, then, that just because a substance is associated, for example, with an increased risk of cleft palate, that doesn't mean that it will also increase the risk of cleft lip with or without cleft palate.
>
> A. That's correct.

(Sep. 25, 2018 Sadler Dep. at 59:2-16). As the Court understands Dr. Sadler's testimony, his opinion is that the two phenotypes are distinct to the extent that exposure to a substance may

cause one phenotype and not the other, but that exposure to a substance can also cause both by a common mechanism.

In his report, Dr. Sadler opined that Zofran can affect the development of the first pharyngeal arch, which "is responsible for forming most of the facial region, including the maxilla, mandible, and the secondary palate," thus leading to "a variety of orofacial defects." (Sadler Report at 22-23). And at his September 25, 2018 deposition, he stated again that Zofran "can affect the first arch during development, and the first arch contributes to much of facial development, so you can have cleft lip, cleft palate." (Sep. 25, 2018 Sadler Dep. at 26:25-27:3). Therefore, it appears to be his opinion that while a substance that causes isolated cleft palate may not always cause cleft lip with or without cleft palate, Zofran can cause both phenotypes of orofacial injury by a common mechanism. Accordingly, Dr. Sadler did not concede a lack of general causation evidence in cases alleging injuries of cleft lip with or without cleft palate, and instead there is a disputed issue of fact as to that issue.

b. <u>Dr. Carol Louik</u>

Dr. Carol Louik is an epidemiologist whose "research focuses on the environmental causes of birth defects in humans." (Louik Report at 1). She has also been hired as an expert for plaintiffs.

GSK contends that Dr. Louik has admitted there is a lack of evidence that Zofran can cause cleft lip with or without cleft palate. First, it says that she has conceded the two phenotypes of orofacial defects are "distinct" for the purposes of causation. Second, it contends that she has not found evidence that Zofran can cause cleft lip with or without cleft palate.

It is true that Dr. Louik made both those concessions. Unlike Dr. Sadler, she plainly admitted that the two orofacial phenotypes are distinct for causation purposes, and that she only found evidence that Zofran can cause isolated cleft palate:

> Q. Okay. And just to clarify, your opinion is that the epidemiological evidence currently only supports an association with isolated cleft palate, right? There's a distinction between isolated and syndromic, of course.
>
> A. Well, yes. And typically, you know – typically epidemiologists classify orofacial clefts as cleft lip with or without palate, or isolated cleft palate. And I'm speaking specifically about isolated cleft palate.
>
> Q. Actually, I understand what you just said, I just want to know – the terminology is a little confusing. So I understand there are two phenotypes, cleft lip with or without cleft palate, and cleft palate only. And you would agree, I think, that they are etiologically and pathogenetically distinct, correct?
>
> A. As far as we know today, yes.

(Louik Dep. at 33:2-20).

However, Dr. Louik left open the possibility that evidence from other fields could establish that Zofran can cause cleft lip with or without cleft palate. In her report, she said that she had formed an opinion as to whether Zofran can cause birth defects based on the methodology and data that an epidemiologist would use. (Louik Report at 3). She did not claim to have considered the data or methodologies considered by experts in other fields. (*See id.*). She testified similarly at her deposition:

> Q. You haven't reviewed the totality of evidence on Zofran and biological mechanism of action, right?
>
> A. As I said in my report, I did a more limited review. I did an in-depth comprehensive review of the epidemiologic literature, and I did a more limited review of the literature from other fields.

(Louik Dep. at 353:5-12). Later in her deposition, she acknowledged that her field's methodology had led her to a different conclusion than plaintiffs' other experts—specifically, that there was insufficient evidence that Zofran could cause cleft lip with or without cleft palate:

> Q. And you're aware that Dr. Danielsson and other plaintiffs' experts have offered opinions that ondansetron is capable of causing congential [sic] heart defects generally?
>
> A. Right.

Q. And *orofacial clefts generally*?

A. Correct.

Q. And your report went to the limits of what epidemiology addressed, and you addressed what you could based on that, right?

A. Based on the epidemiology, yes.

Q. And based on that, you gave opinions on septal defects and *cleft palate*, right?

A. Correct.

(*Id.* at 365:9-22) (emphasis added). However, she testified that, "if embryologists and teratologists and animal researchers are able to expand the mechanism beyond what the epidemiologists have isolated as the specific defect, then no, there's no violation of [epidemiologic] principles." (*Id.* at 367:9-14). In other words, she stated that she did not find epidemiological evidence that Zofran can cause cleft lip with or without cleft palate, but if such evidence were present in other fields, that would not contradict her opinions.

In any event, even if Dr. Louik did not believe there was evidence in any field that Zofran could cause cleft lip with or without cleft palate, there would still be the testimony of plaintiffs' other experts. At least two of those experts have opined that, based on their fields of expertise, Zofran can cause cleft lip with or without cleft palate. (*See* Danielsson Report at 68; Danielsson Dep. at 36:20-24; Sadler Report at 6; Sadler Dep. at 26:24-27:3). That expert testimony is sufficient to create a genuine dispute as to that issue.

Accordingly, GSK's motion for summary judgment will be denied as to the 48 cases alleging orofacial injuries other than isolated cleft palate.

IV. Conclusion

For the foregoing reasons, defendant's motion for summary judgment based on lack of general causation evidence is GRANTED as to plaintiffs Boswell (15-cv-13940), Griffin-

Sperbeck (17-cv-10097), Guzman (17-cv-11035), Jones (16-cv-11518), and Mandoyan (15-cv-13564), and is otherwise DENIED.

So Ordered.

/s/ F. Dennis Saylor IV
F. Dennis Saylor IV
United States District Judge

Dated: October 23, 2019